HUMANITARIAN DEVICE EXEMPTION (HDE) REGULATION
QUESTIONS AND ANSWERS

1. When does FDA make the determination that the disease or condition "affects or is manifested in fewer than 4,000 individuals in the United States per year?

   FDA makes this determination at the time the request for humanitarian use device (HUD) designation is submitted and again each time a request for extension is submitted. FDA will not withdraw approval of an HDE solely because it is subsequently determined that the disease or condition for which the HUD is intended affects or is manifested in more than 4,000 people in the United States per year. This fact may, however, serve as a basis for disapproving an extension request.

2. Would an HDE be approved if the applicant establishes that the affected patient population is fewer than 4,000 per year, but each patient may require numerous devices?

   FDA recognizes that, in some cases, the number of patient contacts with a device may exceed one per patient. Such devices may still qualify for HUD designation as long as the total number of patients treated or diagnosed with the device is less than 4,000 per year in the United States.

3. What is meant by the requirement that no comparable device is available to treat or diagnose the disease or condition?

   One of the criteria that must be satisfied in order for a device to receive marketing approval under this regulation, is that no comparable device, other than another HUD approved under this regulation or a device being studied under an approved IDE, is available to treat or diagnose the disease or condition. Thus, FDA may still approve a device under the HDE regulation even if a comparable device is available under an HDE or IDE. Once a device with the same intended use as the HUD is approved through the premarket approval (PMA) or premarket notification (510(k)) process, an HDE cannot be granted for the HUD device. HDE applicants who have already received marketing approval could continue to market their devices for the duration of their 18 month approval. However, availability of such a comparable device would prohibit the approval of an extension request.

   A "comparable device" need not be identical to the device that is the subject of the HDE application. In determining whether a "comparable device" exists, FDA will consider the device's intended use, technological characteristics, as well as the patient population to be treated or diagnosed with the device. FDA will then decide if an alternative device exists to meet the needs of the identified patient population.

4. How should an HDE applicant verify that the price to be charged does not exceed the costs of research and development, fabrication, and distribution?

   If the amount to be charged is $250.00 or more, FDA requires an HDE applicant to obtain a report by an independent certified public accountant, or in lieu of such a report an attestation by a responsible individual of the organization, verifying that the amount to be charged does not exceed the costs of research, development, fabrication, and distribution. If the amount to be charged is $250.00 or less, FDA will waive this requirement. FDA will, however, allow an HDE applicant to receive incidental profits that exceed the applicant's good faith estimates of costs.

5. How long does FDA have to review an original HDE application?

   The agency has 75 days to review an HDE application from the time such application is received. This includes a 30 day filing period in which the agency determines whether the HDE application is sufficiently complete to permit substantive review. If, however, FDA notifies the HDE applicant that the agency refuses to file the HDE because the application is incomplete, the 75 day timeframe will be extended to include the number of days it takes for the HDE applicant to submit the information the agency believes is necessary to permit substantive review of the application.

6. Will the Quality Systems Regulation (previously known as the Current Good Manufacturing Practice Regulation) apply to HDE applicants?

   Yes. The agency will, however, focus primarily on those manufacturing practices the agency deems most relevant to the safety of the device.

7. Can an HDE applicant request an exemption from the Quality Systems Regulation?

   Yes. An HDE applicant or holder who believes that he/she cannot comply or should not be held to GMP standards may request an exemption from the Quality Systems Regulation. In evaluating such GMP exemption requests, FDA will give overriding consideration to the risks posed by the device, the potential risks that a manufacturing defect might pose to patients, and the public health need for the device.

8. How does the FDA Modernization Act affect the marketing term for an approved HDE application?

   The new law has removed the requirement for applicants to request an extension of approval every 18 months. Additionally, the new law removed the 5 year expiration of the HDE provisions.

9. Are HDE amendments and supplements subject to the same regulations and time periods as those for PMAs?

   HDE amendments and supplements are subject to the same regulations as those for PMAs

except, in accordance with the HDE regulation, an applicant seeking a new indication for use of an already approved HUD shall obtain a new designation of HUD status and shall submit an original HDE. An application for a new indication for use may incorporate by reference any information or data previously submitted to FDA under an HDE.

The review timeframe for HDE amendments and supplements is 75 days, the same as for HDE originals, except for supplements submitted under 21 CFR 814.39(e).

10. Are HDE holders required to submit to FDA the names and addresses of reviewing IRBs?

HDE holders are not required to submit to the agency the names and addresses of reviewing IRBs.

11. Who is responsible for ensuring that a HUD is not administered to or implanted in a patient prior to obtaining IRB approval at a health care facility?

The HDE holder is responsible for ensuring that the HUD is only used in facilities that have established local IRBs. Local IRBs may, however, defer in writing to another similarly constituted IRB that has agreed to assume responsibility for review of the use of the HUD.

12. What types of reviews are IRBs responsible for?

IRBs are responsible for initial as well as continuing review of the HUD.

13. Does an Institutional Review Board (IRB) have to review and approve <u>each</u> individual use of the humanitarian use device (HUD)?

No. The IRB has the discretion to approve use of the HUD as it sees fit, e.g., the IRB may approve the use of the device in general, for groups of patients meeting certain criteria, or for devices under a treatment protocol. If it so wishes, an IRB may specify limitations on the use of the device based upon any criteria it determines to be appropriate.

14. Is informed consent required when treating/diagnosing a patient with a HUD?

The Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 301 *et. seq.*) and the regulation do not require informed consent because an HDE provides for marketing approval and does not constitute research or an investigation which would normally require informed consent. Although the final regulation does not require informed consent, there is nothing in the act or regulation that preempts a State or institution from requiring such consent. If, however, the HUD is the subject of a clinical investigation, i.e., safety and effectiveness data will be collected to support a premarket approval application or publication in a scientific journal, informed consent is required. (21 CFR part 50).